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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,162	03/08/2001	Robert Getts	4081.005	6213

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,162	GETTS, ROBERT	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action filed on April 12, 2005 has been entered.

Status

2. New claims 27-34 are added. Claims 1-34 are pending. All arguments have been fully considered and thoroughly reviewed, and are deemed persuasive for the reasons that follow. This action is made Non- Final.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5,853,993) in view of Nilsen et al. (USPN. 5, 487,973).

Dellinger et al. teach a method claim 1-2 and 18, for detecting nucleic acids on a solid support, wherein the method comprises

1) (a) taking an immobilized capture probe (see column 4, lines 50-67, column 3, lines 44-50);

(b) taking a first component comprising DNA reagents (target analyte comprising mRNA having a capture sequence (homopolymeric tailing or Poly A or poly U tail) (see column 3, lines 20-24, column 5, lines 4-14);

(c) taking a second component (reporter probe) comprising having at least on first arm comprising label and at least one second arm having a second nucleotide sequence which is complementary to the homopolymeric region on the target analyte (see

column 5, lines 23-32, column 10, lines 21-49),wherein said second sequence binds with the capture sequence (homopolymeric region) of the target analyte forming reporter-analyte hybrid (see column 1, lines 53-61);

2) mixing said first and second components at a temperature and for a time sufficient to enable said first component to bind with the second component (see column 1, lines 53-61, column 10, lines 51-57);

3) incubating this mixture with said immobilized capture probe to enable the first nucleotide sequence to bind to said first component, generating a hybridization pattern (see column 1, lines 61-63, column 10, lines 55-60);

with regard to claim 7-8, Dellinger et al. teach that the time sufficient to enable the second and first component is 1 hour to 3 hours (see column 10, lines 52-55);

with regard to claim 10, Dellinger et al. disclose that the detection of the hybridization signal by scanning the microarray using fluoroimager instrument (see column 10, lines 61-62);

With regard to claim 3-4, 11-17, 24-26, Dellinger et al. also disclose washing the microarray to purge unattached reporter probes after hybridization reaction (see column 10, lines 58-60, column 9, lines 30-34);

With regard to claim 5-6, 9, 13, Dellinger et al. teach that the method comprises hybridization buffer (see column 10, lines 51-55);

With regard to claims 20-21, the mixing of first and second components is conducted on the said microarray or in solution (off microarray) (see column 4, lines 50-66).

However, Dellinger et al. did not teach use of dendrimer nucleotide sequences.

Nilsen et al. teach a method of claims 1-26, for detecting a specific nucleic acid in a target sample using a dendrimeric probe wherein Nilsen et al. teach that the method comprises (i) contacting a bead having specific probe sequences with a mixture containing a first component comprising labeled target nucleic acid (DNA or RNA) having a capture sequence and a second component comprising a dendrimer having at least one arm with a nucleotide sequence complementary to the capture sequence of the first component (see column 14, lines 30-35, column 15, lines 37-63); (ii) mixing the first and second components at a temperature to form a bridge between the two components to enable the cross-linking of first component to the second (see column 16, lines 8-11); and incubating the bound mixture with the said bead and detecting signal as an indication of the binding of the target sequence to the specific probe sequence on the bead (see column 16, lines 12-67, column 18, lines 27-51). Nilsen et al. also teach that the method comprises annealing times ranging from 8 minutes (see column 20, lines 24-44) to overnight to 2-6 weeks (see column 3, lines 49-60); detection of hybridization pattern includes detecting the detectable signal (see column 20, lines 38-40); the method comprises hybridization buffer (see column 19, lines 14-26); the unbound dendrimers were removed by a washing step (see column20, lines 35-37); and the isolation of nucleic acid includes spin column (see column20, lines 17-19).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for using microarray hybridization as taught by Dellinger et al. with a method for detecting a nucleic acid sequence using dendrimer as taught by Nilsen et al. to achieve expected advantage of developing an enhanced sensitivity of detecting a target nucleic acid because Nilsen et al.

states that "background noise could be generated in conventional assay not only from binding to a solid support, but also from binding of the probe to nonhomologous DNA sequences. An open branching of a dendrimeric DNA have many degrees of freedom in their movement relative to each other and have a high avidity for DNA that is complementary to the non-annealed single stranded sequences (see column 18, lines 14-26, column 7, lines 14-19). An ordinary practitioner would have been motivated to combine the method of Dellinger et al. with the step of adding dendrimeric probe as taught by Nilsen et al. in order to achieve the expected advantage of developing a sensitive method for detecting a target nucleic acid because the addition of the limitation as taught by Nilsen et al. would reduce non-specific binding and reduce background noise and enhance specific hybridization signal. Transcribing a RNA target to a cDNA represents routine optimization with regard to hybridization assays using DNA, which routine optimization parameters are explicitly recognized in Nilsen et al.. As noted in *In re Aller*, 105 USPQ 233 at 235,More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable conditions by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the utilization of reverse transcription reagents selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

B. Claims 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5,853,993) in view of Nilsen (USPN. 5, 487,973).

as applied to claims 1-26 above, and further in view of Landers et al. (USPN.6,246,046).

Dellinger in view of Nilsen et al. teach a method for detection and assay on a microarray as discussed above in section 3A.

Neither Dellinger et al. nor Nilsen et al. teach use of a dual or multi channel hybridization assay as claimed in claims 27-34.

Landers et al. teach the use of multi channel or capillary array or matrix hybridization array chips which facilitate rapid scanning, comprising up to 200 densely-packed micro-channels or capillaries scanned in less than a millisecond (see col. 3, line 65-67, col. 4, line 1-35). Landers et al. also teach that the use of multi-channel hybridization assay provides a high speed, high resolution micro-channel monitoring system fro multi-functional capillary electrophoresis on a single chip and is applicable for high throughput assay applications (see col. 4, line 35-42).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for using micro array hybridization as taught by Dellinger et al. in view of Nilsen et al. with a high throughput multichannel hybridization assay format to achieve expected advantage of developing a high throughput, high speed method for enhanced sensitivity of detecting multiple target nucleic acids on a single microarray .An practitioner would have been motivated to combine the method of Dellinger et al. in view of Nilsen et al. with the step of adding a multi-channel hybridization assay format as taught by Landers et al for the purpose of detecting multiple target nucleic acids in a short time with high resolution in a high throughput acid because Landers et al. explicitly taught that the use of multi-channel hybridization assay provides a high speed, high resolution micro-channel monitoring

system for multi-functional capillary electrophoresis on a single chip and is applicable for high throughput assay applications (see col. 4, line 35-42) and such modification is considered obvious over the cited prior art in the absence of secondary considerations.

Response to arguments:

Applicants' arguments with regard to the rejection made in the previous office action under 35 USC 103(a) are fully considered and found persuasive in part. Applicants' correctly pointed out that citations of Nilsen reference (USPN. 6,274,723) do not support Examiner's assertions. Examiner notes that it was an error. The reference USPN. 6,274,723 was not correctly cited in the last Office action. The correct number of the Nilsen patent is USPN. 5,487,973 and the citations are from the USPN. 5,487,973. The correct citation is shown on the attached PTO-892. The rejection is re-written to correct the USPN. Number of Nilsen reference (note the text in the above rejection is not modified).

Further Applicants argue that with regard to the Dellinger et al. reference, Examiner has not shown citations for claims 2 and 22 which utilize reverse transcriptase and RT primer having the capture sequence. Applicants' arguments are fully considered and found not persuasive because the cDNA reagents cited by Dellinger et al. comprise a RNA target and it is considered as a routine optimization condition to use of reverse transcriptase and RT primer (oligo dT primer)to transcribe a RNA target into a cDNA which can be used in a mnner as taught by Nilsen et al. since Nilsen et al. explicitly taught that dendrimeric probe has high avidity towards a DNA target. Further, Applicants also argue that the Nilsen patent does not disclose use of spin column. Theses arguments are not persuasive. As discussed above to the correct USPN. 5,487,973 does teach use of

spin columns. Examiner also notes that Applicants' arguments are based on attacking each reference independently. According to MPEP 2145 One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, specific motivation is provided in the rejection above, and an ordinary practitioner would be motivated to modify the method for using microarray hybridization as taught by Dellinger et al. with a method for detecting a nucleic acid sequence using dendrimer as taught by Nilsen et al. to achieve expected advantage of developing an enhanced sensitivity of detecting a target nucleic acid because Nilsen et al. states that "background noise could be generated in conventional assay not only from binding to a solid support, but also from binding of the probe to nonhomologous DNA sequences. An open branching of a dendrimeric DNA have many degrees of freedom in their movement relative to each other and have a high avidity for DNA that is complementary to the non-annealed single stranded sequences (see column 18, lines 14-26, column 7, lines 14-19). An ordinary practitioner would have been motivated to combine the method of Dellinger et al. with the step of adding dendrimeric

probe as taught by Nilsen et al. in order to achieve the expected advantage of developing a sensitive method for detecting a target nucleic acid because the addition of the limitation as taught by Nilsen et al. would reduce non-specific binding and reduce background noise and enhance specific hybridization signal. The rejection is maintained herein and the rejection is re-written to incorporate correct reference number of Nilsen patent, (note that the text is not changed).

4. The rejections under provisional double patenting with the co-pending applications 09/ 908,950, and 10/234, 069 are maintained herein. Applicants' arguments are fully considered and the arguments are found not persuasive. In response to the request for the co-pending application details, Examiner herewith provide the details in PTO-892 form. The rejection for 10/ 050,088, is withdrawn herein, since the case is now abandoned. The instant claims encompass the limitations of the claims in the above co-pending applications and therefore the rejections are maintained herein until a terminal disclaimer is submitted.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
Examiner, Art Unit 1637

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